

PRELIMINARY REMARKS

Claims 17, 18, 21 to 23, 28 to 31, 34 to 42, and 46 to 52 as set forth in the Listing of the Claims presented on April 25, 2011, are currently pending. No Claim(s) is(are) canceled, amended, or added herewith. Of the pending claims, Claims 17, 18, 22, 23, 31, 34, 38 to 42, 46, 49 and 52 stand withdrawn from consideration, and Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51 stand rejected.

More specifically, Claims 21, 28 to 30, 35 to 37, 47, 48, 50 and 51 were rejected as allegedly being unpatentable

- a) under 35 U.S.C. §103(a) in light of the teaching of *von Deyn et al.* (WO 96/26206 which corresponds to US 5,846,907) when taken in view of the disclosure of *Silverman* (The Org. Chem. of Drug Design and Drug Action, Academic Press, Inc. San Diego, 1992, pp. 4-51), and
- b) under the judicially created doctrine of obviousness-type patenting in light of Claims 1 to 8 of *von Deyn et al.* (id.) when taken in view of the disclosure of *Silverman* (id.).

For the reasons set forth in the following, and in light of the enclosed Declaration of Dr. Witschel dated December 14, 2011, the subject matter of applicants' claims is not deemed to be rendered unpatentable by the referenced art. As the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. §103 obviousness determination, *e.g.*, *In re Braithwaite*, 379 F.2d 594 (CCPA 1967); *In re Longi*, 759 F.2d 887 (Fed. Cir. 1985); *In re Braat*, 837 F.2d 589 (Fed. Cir. 1991), the following remarks are equally applicable to both of the rejections.

The rejections *inter alia* rely on the disclosure of *Silverman* as supporting that one would reasonably expect the replacement of a substituent of a compound by a classical isostere of the substituent to yield a compound having similar utility. According to *Silverman*, the structural modification of a lead compound along the lines of bioisosterism “has been shown to be useful to attenuate toxicity or to modify the activity of a lead, and it may have a significant role in the alteration of metabolism of a lead[.]” see page 19, sect. 4, 2nd sentence. Additionally, *Silverman* explains the distinction which has to be made between the activity and the potency of a

compound, stating, “*Activity is the particular biological or pharmacological effect (e.g., antibacterial activity or anticonvulsant activity); potency is the strength of that effect.*” See page 8, para. 1, 5th sentence (*emphasis original*). Notwithstanding the fact that Silverman cite a reference for providing that “*Bioisosters are substituents or groups that have chemical or physical similarities, and which produce broadly similar biological properties*”, see page 19, sect. 4., 1st sentence (*emphasis original*), when stating that a bioisosteric replacement may modify the *activity* of a compound, **Silverman** in fact confirms that there is no reasonable expectation that the utility of a compound resulting from such a replacement is similar to that of the compound from which it is derived, *cf.* Dr. Witschel’s Declaration pages 4-5. In this context it is also deemed notable that **Silverman** mention that a replacement of a group along the lines of bioisosterism may attenuate toxicity. A herbicidal effect results when a compound is phytotoxic to plants. Thus, a structural modification which attenuates the toxicity of a herbicide is not per se desirable. Moreover, as addressed by Dr. Witschel in the Declaration in the section starting with the last paragraph on page 5, replacing an ortho chloro-substituted phenyl group by an ortho methyl-substituted phenyl group in the context of herbicidal compounds is known to attenuate the toxicity of herbicides, i.e., it dramatically reduced the herbicidal effect in the case of the herbicides addressed in **US 4,405,357**.

The disclosure of **Silverman**, therefore, is deemed unsuited to support the proposition that one would reasonably expect the replacement of a substituent of a compound by a classical bioisostere of the substituent to result in a compound having similar utility. Moreover, the respective disclosure, especially when taken together with the background knowledge of those in the herbicidal art as illustrated by the teaching of **US 4,405,357**, is deemed unsuited to motivate one of ordinary skill in the art to replace the 2-chlorophenyl group of **von Deyn et al.**’s compounds 5.4 and 5.5 by a 2-methylphenyl moiety. In particular, in consideration of the disclosure of **Silverman** and, e.g., the teaching of **US 4,405,357**, one having ordinary skill in the herbicidal art could not reasonably expect that replacing the 2-chlorophenyl group of **von Deyn et al.**’s compounds 5.4 and 5.5 by a 2-methylphenyl moiety would yield compounds which exhibit a higher potency against unwanted plants while, at the same time, being less phytotoxic to crop plants, *cf.*, Dr. Witschel’s Declaration page 6. The teaching of **von Deyn et al.** itself, at best, merely conveys that replacing one of the radicals in the position designated as “M” of the prior art compounds by another radical within the definition of “M” is of little consequence. As

such, the teaching of *von Deyn et al.* also fails to reasonably support that one having ordinary skill in the herbicidal art could reasonably expect the 2-methyl-substituted compounds according to applicants claims to be more potent herbicides while, at the same time being less phytotoxic to crop plants, than the corresponding 2-chloro-substituted compounds 5.4 and 5.5 of *von Deyn et al.*

The rejections also rely on the disclosure of *Silverman* for supporting that the structural modification of known compounds is routinely done in order to optimize utility.

On the one hand, it should be noted that a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 620 (CCPA 1977). Nothing in the teaching of *von Deyn et al.* or the disclosure of *Silverman* suggests that the nature of the group which takes the position of “M” in *von Deyn et al.*’s compounds is a result effective parameter in the context of the prior art compounds in general, or in the context of prior art compounds 5.4 and 5.5 in particular.

On the other hand, *Silverman* explains that the optimization of a lead compound using the approaches addressed in the reference is a fairly random process, *see* page 47, sect. G, 1st sentence. Under certain circumstances, what is “*obvious to try*” may be equated with obviousness, namely, where the prior art provided a finite number of identified, predictable potential solutions to a recognized need or problems. *See KSR Int’l v. Teleflex, Inc.*, 550 U.S. 398, 421 (2007). However, “*“obvious to try” is erroneously equated with obviousness under Section 103(a) where ‘what would have been “obvious to try” would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.’” See In re Kubin*, 561 F.3d 1351, 1359 (2009) (quoting *In re O’Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)). The teaching of *von Deyn et al.* and the disclosure of *Silverman* fail to reasonably suggest which of the various structural parameters of the prior art compounds may be effective with a view to the properties of the compounds. Thus, one having ordinary skill in the herbicidal art would have

had to vary all parameters and try each of numerous possible choices until possibly arriving at an improved herbicide.

Moreover, as previously submitted by applicants, Section 103(a) specifically provides: “*Patentability shall not be negated by the manner in which the invention was made.*” That is, the path that leads an inventor to the invention is expressly made irrelevant to patentability by statute. In fact, the Court has acknowledged, “*Most technological advance is the fruit of methodical, persistent investigation as is recognized in 35 U.S.C. §103 (‘patentability shall not be negated by the manner in which the invention was made’).*” *In re Dow Chemical Co.*, 837 F.2d 469, 472 (Fed. Cir. 1988). Thus, it is irrelevant in the determination under Section 103(a) that one may be able to find compounds exhibiting “optimized” properties by structural modification of the compounds of *von Deyn et al.* using routine experiments and ordinary skill.

The rejections further asserted that the data and results which were presented with Dr. Witschel’s Declarations of October 21, 1999, were insufficient or inadequate to show the unexpected and beneficial properties of the compounds disclosed and claimed by applicants as compared to the compounds of *von Deyn et al.* Enclosed herewith applicants submit a further Declaration of Dr. Witschel which explains in detail why the data and results provides in the earlier Declarations, when considered as a whole, corroborate

- that the structural modification which distinguishes applicants’ compounds from those disclosed by *von Deyn et al.* conveys superior and unexpected properties to applicants’ compounds;
- that the data and results which were obtained in investigations which did not involve one of the prior art compounds 1.79, 5.4, or 5.5, are equally important when assessing the superior and unexpected properties of applicants’ compounds as those data and results further illustrate the trends which are apparent in the herbicidal properties of applicants’ compounds;
- that the unexpected and superior properties of applicants’ compounds are of practical value; and
- that the data and results allow an assessment of the unexpected and superior properties of applicants’ compounds even without the indication of standard deviations and like statistical values.

Together with the Declaration, applicants have enclosed a separate and enlarged copy of the photographs set forth on pages 15-17 of the Declaration which may be better suited to show the significant differences in plant development and damage which result in the different ratings assigned in each case.

In light of the foregoing and the attached, as well as applicants' remarks in their paper of April 25, 2011, it is respectfully urged that the subject matter of applicants' claims is patentable in light of the teaching and the claims of *von Deyn et al.*, taken alone or taken in view of the disclosure of *Silverman*. It is therefore respectfully requested that the respective rejections be withdrawn. Favorable action is solicited.

CONCLUSION

The foregoing shows that the subject matter of applicants' claims is patentable under the pertinent provisions of the statute, and that the claims are in good condition for allowance. In order to facilitate the resolution of any remaining issues or questions presented by this paper, applicants respectfully request that the Examiner directly contact the undersigned by phone to further the discussion. Favorable action is solicited.

Respectfully submitted,

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Encl.: Dr. Witschel's Declaration of December 14, 2011
Enlarged copy of photographs